A Novel Inhibitory Receptor of Platelets

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Keywords: Therapeutic, Diagnostic, Cancer, Immune disorders, Antibody, Platelets, Thrombin

Background:
The National Cancer Institute's Molecular Targets Laboratory is seeking statements of capability or interest from parties interested in collaborative research on a novel, inhibitory platelet surface protein known as TREM like Transcript (TLT-1). The collaborative research would be pre-clinical development of a potential therapeutic target for thrombosis and other platelet-associated disorders, as well as immune disorders.

Technology:
Triggering Receptors in Myeloid Cells (TREM) modulate innate and adaptive immunity. Specifically, TREM1 amplifies the response to sepsis in innate immunity by activating neutrophils and other leukocytes. TREM2 potentiates dendritic cell maturation in adaptive immunity. This discovery implies the receptor has an important regulatory role in both innate and adaptive immunity. TLT-1 is a potential therapeutic target for thrombosis and other platelet-associated disorders, as well as immune disorders, cancer, septic shock, infectious disease, stroke, heart disease, myocardial infarction, vascular disorders. Detection of soluble TLT-1 in patient plasma suggests the protein is a marker of ongoing coagulopathies. Defective platelet aggregation in TLT-1 null mice confirms a role for the protein in regulation of thrombosis associated with inflammation. The target validation is complete. TLT-1 null mice demonstrate defects in platelet aggregation with no gross bleeding defect.

Applications:
- TLT-1 has potential as a therapeutic target for thrombosis and other platelet-associated disorders, as well as immune disorders, cancer, septic shock, infectious disease, stroke, heart disease, myocardial infarction, vascular disorders.
- Complete human origin of these antibodies suggests negligible immunogenicity and minimizes the problem of adverse immune responses in human therapy.

Development Status: *In vivo* studies ongoing.

Reference: "Inhibition of thrombin-induced platelet aggregation using human single-chain Fv antibodies specific for TREM-like transcript-1" Giomarelli, B., Washington, V.A., Chisholm, M.M., Quigley, L., McMahon, J.B., Mori, T., McVicar, D.W. Thromb Haemost 2007; 97: 955–9 [PubMed abstract].

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